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**BURNS DOANE**

BURNS DOANE SWECKER & MATHIS LLP  
ATTORNEYS AT LAW

ALEXANDRIA, VIRGINIA  
REDWOOD SHORES, CALIFORNIA  
DURHAM, NORTH CAROLINA

**REPLY TO:**  
P.O. Box 1404  
Alexandria, Virginia 22313-1404

**TELEPHONE:** +1.703.836.6620

**FACSIMILE:** +1.703.836.2021 (Group 3)  
+1.703.836.0028 (Group 4)

**DATE:** May 6, 2002

RECIPIENT INFORMATION	SENDER INFORMATION
To: <b>Ex. Goldberg</b>	From: <b>Dawn Gardner, Reg. No. 44,118</b>
Voice Tel. No.:	Voice Tel. No.: <b>(703) 838-6692</b>
Fax Tel. No.: <b>(703) 746-5149</b>	Sent By: <b>DMG</b>
Your Ref.: <b>09/462,635</b>	Our Ref.: <b>020600-285</b>
	Total Pages (Incl. Cover Page): <b>9</b>

**RE:**

**MESSAGE:**

Dear Examiner Goldberg,

Attached is a draft Amendment and Reply after final for your review. We will discuss the proposed amendments in our interview scheduled for tomorrow, May 7, 2002, at 10 a.m.

Best Regards,  
Dawn Gardner

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(BDSM 05/01)

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**DRAFT**

Patent

Attorney's Docket No. 020600-285**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Patent Application of )  
SCHMIDT et al ) Group Art Unit: 1655  
Application No.: 09/462,635 ) Examiner: J. A. Goldberg  
Filed: April 10, 2000 )  
For: CATEGORISING NUCLEIC ACID )  
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**AMENDMENT AND REPLY PURSUANT TO 37 C.F.R. § 1.116**

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

In complete response to the Final Official Action mailed on December 21, 2001, in connection with the above-identified application, applicants provide the following amendments and remarks.

**In The Claims:**

Please amend claim 14 as follows:

14. (Twice Amended) A method for categorizing nucleic acid, wherein said method comprises:

(i) digesting double-stranded nucleic acid with an endonuclease to produce a nucleic acid population, wherein said endonuclease is selected such that each nucleic acid in the resulting nucleic acid population has a sticky end of a known base sequence and of a

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known common length extending from a terminal of its double-stranded portion, and wherein each nucleic acid in the nucleic acid population has a double-stranded portion;

(ii) contacting the nucleic acid population with an adaptor to ligate the adaptor to a terminal of each nucleic acid in the nucleic acid population, wherein said adaptor comprises a double-stranded primer portion having a known base sequence, and a single-stranded portion complementary to the known sticky end of the nucleic acids in the nucleic acid population;

(iii) categorizing the nucleic acid by isolating a nucleic acid wherein both termini of the double-stranded portion of said nucleic acid correctly hybridize to an oligonucleotide sequence by

(a) dividing the nucleic acid population into a plurality of separate wells;

(b) contacting a first set of oligonucleotide sequences with the nucleic acid population by adding to each well a different oligonucleotide from the first set of oligonucleotide sequences;

(c) denaturing the nucleic acid population in the presence of the first set of oligonucleotide sequences to produce a single-stranded nucleic acid population and allowing the single-stranded nucleic acid to hybridise to the first set of oligonucleotide sequences, wherein each oligonucleotide sequence in said first set of oligonucleotide sequences has a pre-determined recognition sequence, the nucleic acid being categorized by its ability to correctly hybridize to oligonucleotide sequences having the recognition sequence, the recognition sequence being situated such that it recognizes a sequence in the portion of the nucleic acid which was double-stranded after digestion with the endonuclease;

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(d) immobilizing in each well those nucleic acids which correctly hybridise to the first sequences;

(e) extending the correctly hybridised oligonucleotide sequences along the single-stranded portion of the immobilised nucleic acid to form double-stranded nucleic acid;

(f) denaturing the double-stranded nucleic acid and removing non-immobilised species to isolate the resulting immobilised single-stranded nucleic acid;

(g) contacting the immobilised single-stranded nucleic acid with a second set of oligonucleotide sequences, by adding to each well a different oligonucleotide from the second set of oligonucleotide sequences, wherein each oligonucleotide sequence in said second set of oligonucleotide sequences has a pre-determined recognition sequence, the nucleic acid being categorized by its ability to correctly hybridize to oligonucleotide sequences having the recognition sequence, the recognition sequence being situated such that it recognizes a sequence in the portion of the nucleic acid which was double-stranded after digestion with the endonuclease;

(h) extending the correctly hybridised oligonucleotide sequences in each well along the immobilised single-stranded nucleic acid to form double-stranded nucleic acid;

(i) denaturing the double-stranded nucleic acid; and

(j) isolating the resulting non-immobilised single-stranded nucleic acid from each well, thereby sorting the nucleic acid population into a plurality of sub-populations.

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Page 4**REMARKS**

Entry of the foregoing and further and favorable reconsideration of the subject application, in view of the following remarks and pursuant to 37 C.F.R. § 1.116, are respectfully requested. By the present amendment, claim 14 has been amended to indicate that the nucleic acid population is sorted into separate populations in separate wells. Support for these amendments may be found, at the very least, on pages 7 and 8 of the specification as filed. No new matter has been added by the foregoing amendment.

Entry of this Amendment is proper under 37 C.F.R. § 1.116 because the amendment places the application in condition for allowance for the reasons discussed herein; does not raise any new issue requiring further search and/or consideration because the amendments amplify issues previously discussed throughout prosecution; does not present any additional claims; and places the application in better form for an appeal, should an appeal be necessary. Entry of the Amendment is thus respectfully requested.

None of the prior art cited by the Examiner disclose or suggest the features of amended claim 14. Specifically, neither Rothberg et al, Dynal Catalog nor Hartley et al disclose or suggest dividing a nucleic acid population into a plurality of separate wells and adding a different oligonucleotide to each well. The invention as defined in claim 14 allows the physical separation of the nucleic acids, which also permits the process to be repeated on the isolated pool to categorize or physically sort the nucleic acids further with additional oligonucleotides that extend further in the unknown sequence of the sorted nucleic acids. None of the cited references disclose or suggest separating the nucleic acids according to sequence by selective immobilization in separate wells.

new issue  
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considerations.

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Applicants respectfully submit that all of claims 14-22 and 42-49 are now in condition for allowance. Reconsideration and withdrawal of the rejections of the claims under 35 U.S.C. § 103(a) are respectfully requested. Prompt reconsideration and allowance of the claims is believed to be next in order.

Should the Examiner require anything further in order to place the application in better condition for allowance, he is invited to contact applicants representative at the telephone number below.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

**DRAFT**

By: \_\_\_\_\_  
Dawn M. Gardner  
Registration No. 44,118

P.O. Box 1404  
Alexandria, Virginia 22313-1404  
(703) 836-6620

Date:

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Attachment to Amendment and Reply dated

**Marked-up Claim 14**

14. (Twice Amended) A method for categorizing nucleic acid, wherein said method comprises:

(i) digesting double-stranded nucleic acid with an endonuclease to produce a nucleic acid population, wherein said endonuclease is selected such that each nucleic acid in the resulting nucleic acid population has a sticky end of a known base sequence and of a known common length extending from a terminal of its double-stranded portion, and wherein each nucleic acid in the nucleic acid population has a double-stranded portion;

(ii) contacting the nucleic acid population with an adaptor to ligate the adaptor to a terminal of each nucleic acid in the nucleic acid population, wherein said adaptor comprises a double-stranded primer portion having a known base sequence, and a single-stranded portion complementary to the known sticky end of the nucleic acids in the nucleic acid population;

(iii) categorizing the nucleic acid by isolating [a] nucleic [acid] acids wherein both termini of the double-stranded portion of said nucleic acid correctly hybridize to an oligonucleotide sequence by

(a) dividing the nucleic acid population into a plurality of separate wells;  
(b) contacting a first set of oligonucleotide sequences with the nucleic acid population by adding to each well a different oligonucleotide from the first set of oligonucleotide sequences[:]

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Page 2Attachment to Amendment and Reply dated**Marked-up Claim 14**

((a)c) denaturing the nucleic acid population in the presence of the first set of oligonucleotide sequences to produce a single-stranded nucleic acid population and allowing the single-stranded nucleic acid to hybridise to the first set of oligonucleotide sequences, wherein each oligonucleotide sequence in said first set of oligonucleotide sequences has a pre-determined recognition sequence, the nucleic acid being categorized by its ability to correctly hybridize to oligonucleotide sequences having the recognition sequence, the recognition sequence being situated such that it recognizes a sequence in the portion of the nucleic acid which was double-stranded after digestion with the endonuclease;

((b)d) immobilizing those nucleic acids which correctly hybridise to the [first sequences] oligonucleotide sequence added to that well;

((c)e) extending the correctly hybridised oligonucleotide sequences along the single-stranded portion of the immobilised nucleic acid to form double-stranded nucleic acid;

((d)f) denaturing the double-stranded nucleic acid and removing non-immobilised species to isolate the resulting immobilised single-stranded nucleic acid;

((e)g) contacting the immobilised single-stranded nucleic acid with a second set of oligonucleotide sequences, by adding to each well a different oligonucleotide from the second set of oligonucleotide sequences, wherein each oligonucleotide sequence in said second set of oligonucleotide sequences has a pre-determined recognition sequence, the nucleic acid being categorized by its ability to correctly hybridize to oligonucleotide sequences having the recognition sequence, the recognition sequence being situated such



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**Marked-up Claim 14**

that it recognizes a sequence in the portion of the nucleic acid which was double-stranded after digestion with the endonuclease;

([f]h) extending the correctly hybridised oligonucleotide sequences in each well along the immobilised single-stranded nucleic acid to form double-stranded nucleic acid;

([g]i) denaturing the double-stranded nucleic acid; and

([h]j) isolating the resulting non-immobilised single-stranded nucleic acid from each well, thereby sorting the nucleic acid population into a plurality of sub-populations.